Guidelines for Lyme Disease Vaccine Use in California for Health Care Providers

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In February 2002, GlaxoSmithKline (formerly SmithKline Beecham Pharmaceuticals) announced that it will no longer produce or market LYMErix ™, citing poor sales. There is currently no other Lyme disease vaccine approved for use in humans by the United States Food and Drug Administration.

In December 1998, the U.S. Food & Drug Administration (FDA) approved the first Lyme disease vaccine for use in humans. National recommendations on the use of this vaccine by the U.S. Public Health Service Advisory Committee on Immunization Practices (ACIP) were published in June 1999. While the ACIP recommendations provide general guidelines for prudent use of the vaccine, they do not directly address specific circumstances and questions pertinent to the citizens of California. Therefore, the California Department of Health Services has prepared these guidelines in an attempt to provide direction for use of the Lyme disease vaccine in California. ***These guidelines contain recommendations based on general statewide information. For more specific information on Lyme disease or ticks in local areas, individuals should contact their local health department.***

Summary of Guidelines for Use of Human Lyme Disease Vaccine in California

1. **Routine vaccination is not recommended anywhere in California.**
2. **Individuals who have frequent or prolonged contact with natural vegetation (including leaf litter) in tick habitat in areas known to have moderate risk (i.e., more than low or no risk) for Lyme disease (see map) should consider vaccination and discuss the risks and benefits with their physician.**
3. **Use of the vaccine should not deviate from FDA and package insert guidelines for vaccine administration and schedule.**
4. **Vaccination is not a substitute for personal measures to prevent tick bites and tick-transmitted diseases.**

Lyme disease (LD) is a multi-system syndrome caused by the spirochete *Borrelia burgdorferi*. Most persons reported with LD present with early localized disease characterized by an erythema migrans rash that expands over several days, often with central clearing. Symptoms of early disseminated LD, including fever, myalgia, headache, arthralgia, cranial nerve palsy, and atrioventricular conduction defects, may occur concurrent with, days to weeks after, or in the absence of erythema migrans. If left untreated, some persons with LD can develop oligoarthritis and central nervous system dysfunction. Most cases of LD can be effectively treated with antimicrobials; however, long-term complications may develop if diagnosis and treatment are delayed.

Borrelia burgdorferi is transmitted by ticks of the *Ixodes ricinus* complex. Both the nymphal and adult forms of the tick are capable of transmitting the spirochete. In the upper Midwestern and northeastern United States, the vector is the deer tick (*Ixodes scapularis*); in some areas more than 50 percent of adult deer ticks are infected with *B. burgdorferi*. In the West, the vector is the western black-legged tick (*Ixodes*

pacificus). *Ixodes pacificus* ticks have been identified in 56 of California's 58 counties. *Ixodes pacificus* ticks are most common in densely vegetated or wooded areas of the coastal range north of San Francisco, the western Sierra foothills of northern California, and the San Francisco Bay Area including Santa Cruz County; they are less common in the Central Valley and from the Tehachapi Mountains south. The proportion of *I. pacificus* ticks infected with *B. burgdorferi* is comparatively low: approximately 1-2 percent of adult ticks and 5-6 percent of nymphs statewide, based on limited data. This low infection proportion is due to a separate maintenance cycle involving woodrats and the propensity of immature *I. pacificus* to feed on lizards, which are incompetent reservoirs for the spirochete. A few focal *I. pacificus* populations in northern California have been identified in which up to 13 percent of nymphs are infected.

National surveillance for LD was initiated in 1982. The annual number of reported cases rose steadily from 491 in 1982 to a peak of 16,801 in 1998. Nearly 90 percent of the more than 120,000 cases reported nationwide occurred among residents of the Northeast and Upper Midwest. The five states with the highest reported incidence (per 100,000 population) in 1998 were Connecticut (105), Rhode Island (80), New York (25), New Jersey (24), and Pennsylvania (23). The reported incidence in California in 1998 was 0.4 per 100,000 population overall, with the incidence being higher for some north coastal counties.

Prevention of LD involves a multi-pronged approach that includes avoidance of tick-infested areas, chemical control of tick populations, environmental management, and personal protective measures. In December 1998, LYMErix™ (SmithKline Beecham Pharmaceuticals) became the first LD vaccine approved by the FDA for use in this country. LYMErix™ is a recombinant vaccine based on a well-conserved antigen of *B. burgdorferi* known as outer surface protein A (Osp A). The theoretical mechanism of the vaccine is that anti-OspA antibody, ingested during the tick's bloodmeal, will bind with and inactivate spirochetes in the tick's midgut and interrupt spirochetal migration to the salivary gland and transmission to the human host.

The vaccine is administered in three intramuscular injections: at 0, 1, and 12 months. Field trials demonstrated an efficacy of 76 percent in persons who received the full three-dose series. Immunogenicity and efficacy were lower in persons who received only two doses (approximately 50% efficacy) and/or were over 60-65 years of age. Local reactions such as swelling, redness, and soreness at the inoculation site were reported in approximately 25-30 percent of vaccinees. Minimal information is currently available about possible delayed adverse effects of vaccination. The relatively brief experience with these vaccines may not have uncovered severe side effects that could become manifest only years later. For example, while no cases of immune-mediated arthritis have to date been attributed to receiving the LD vaccine, on the basis of animal experiments and theoretical reasoning some investigators have postulated that LD vaccines containing *B. burgdorferi* recombinant Osp A might increase this risk. Currently there is insufficient scientific evidence to verify this potential problem or estimate the level of risk, but physicians should consider including this issue in their discussions with patients on the pros and cons of immunization. Preliminary studies of the vaccine in Europe demonstrated acceptable safety and immunogenicity among children less than 15 years-old, but efficacy studies among children in the United States

have yet to be completed and the vaccine is not currently approved for use in this age group. There have to date been no published safety or efficacy studies of the vaccine in adults more than 70 years old, pregnant women, immunocompromised individuals, or patients with chronic arthritis. Therefore, the vaccine is currently not recommended for individuals in these groups. Recent studies have demonstrated that accelerated dosage schedules--0, 1, 6, and 0, 1, 2--produce comparable immunogenicity, however these regimens are not yet approved by the FDA. Generally, antibodies diminish with time so it is likely that periodic (e.g., annual) boosters will be necessary, but exact booster schedules have not yet been determined. Safety and efficacy studies have also not been published regarding simultaneous administration of the LD vaccine with other vaccines.

Based on current information on vaccine safety and efficacy, and the known epidemiology of LD in California, **the LD vaccine is NOT recommended for routine use anywhere in California.** Decision analysis models indicate that routine administration of the LD vaccine is cost-effective only for populations at much higher risk of LD--i.e., in populations with annual incidence greater than 1,000 cases per 100,000 population.

Although LD cases have been reported from almost every county in California, based on tick studies and the residences of reported cases of LD to date, there are defined geographic areas in this state with *some* or *moderate* risk for LD, relative to the rest of the State where the risk is low or nil. These areas of more than minimal risk include the northern coastal range (*moderate* risk), the western Sierra foothills (*some* risk), and the San Francisco Bay Area including Santa Cruz County (*some* risk) (Figure 1). **LD vaccination should be considered in individuals who have frequent or prolonged exposure (i.e., actual contact) to natural vegetation (including leaf litter) in wooded, brushy, or overgrown grassy habitats WITHIN geographic areas known to have *moderate* risk for LD** (Table 1). Examples of individuals with prolonged and frequent contact are park rangers and persons working daily in such environments. For individuals with exposure in *moderate* risk areas but whose exposures are neither frequent nor prolonged (such as regular weekend hikers who do not usually go off the trails into brushy vegetation), and for individuals with frequent and prolonged exposure but in areas with *some* risk, LD vaccine may be considered; **however, the benefit of vaccination beyond that provided by basic personal protective measures and early diagnosis and treatment of infection is uncertain**. Persons considering LD vaccination should consult with their health care provider about the benefits and potential risks of LD vaccination. Risk should be assessed on an individual basis, considering the density and prevalence of infected *I. pacificus* ticks in the environment, and the potential for person-tick contact. LD vaccine is **NOT** recommended for persons with exposure (frequent or infrequent) to vegetation in low or no risk areas of the State (see map).

Vaccine administration and schedule should not deviate from FDA and package insert guidelines. LYMErix™ (SmithKline Beecham Pharmaceuticals) should be administered intramuscularly as a three-dose series, with the second and third dose given one and 12 months, respectively, after the first dose.

It is important to note that the LD vaccine offers protection against only infection with *B. burgdorferi* and that even this protection is not 100 percent. There is no evidence yet to suggest that use of the vaccine in California (or elsewhere, for that matter) is of proven benefit beyond measures to prevent tick bites. The decision to vaccinate will depend on an objective evaluation of individual risks for LD and the physician's discussion with individual patients about the risks, benefits, and present limitations of the vaccine. Persons who, after consultation with their physician, elect to receive the vaccine remain at risk for other tick-transmitted diseases known to occur in California, most especially ehrlichiosis and babesiosis. **LD vaccine is NOT a substitute for measures to prevent tick bites**. Individuals should practice the following personal protective measures as the most effective means of decreasing the risk of all tick-borne diseases: avoid areas with high tick populations, wear appropriate clothing, use repellants, conduct tick checks, and promptly remove any attached ticks.

Table 1. SUMMARY OF DHS GUIDELINES FOR USE OF THE LYME DISEASE VACCINE IN CALIFORNIA

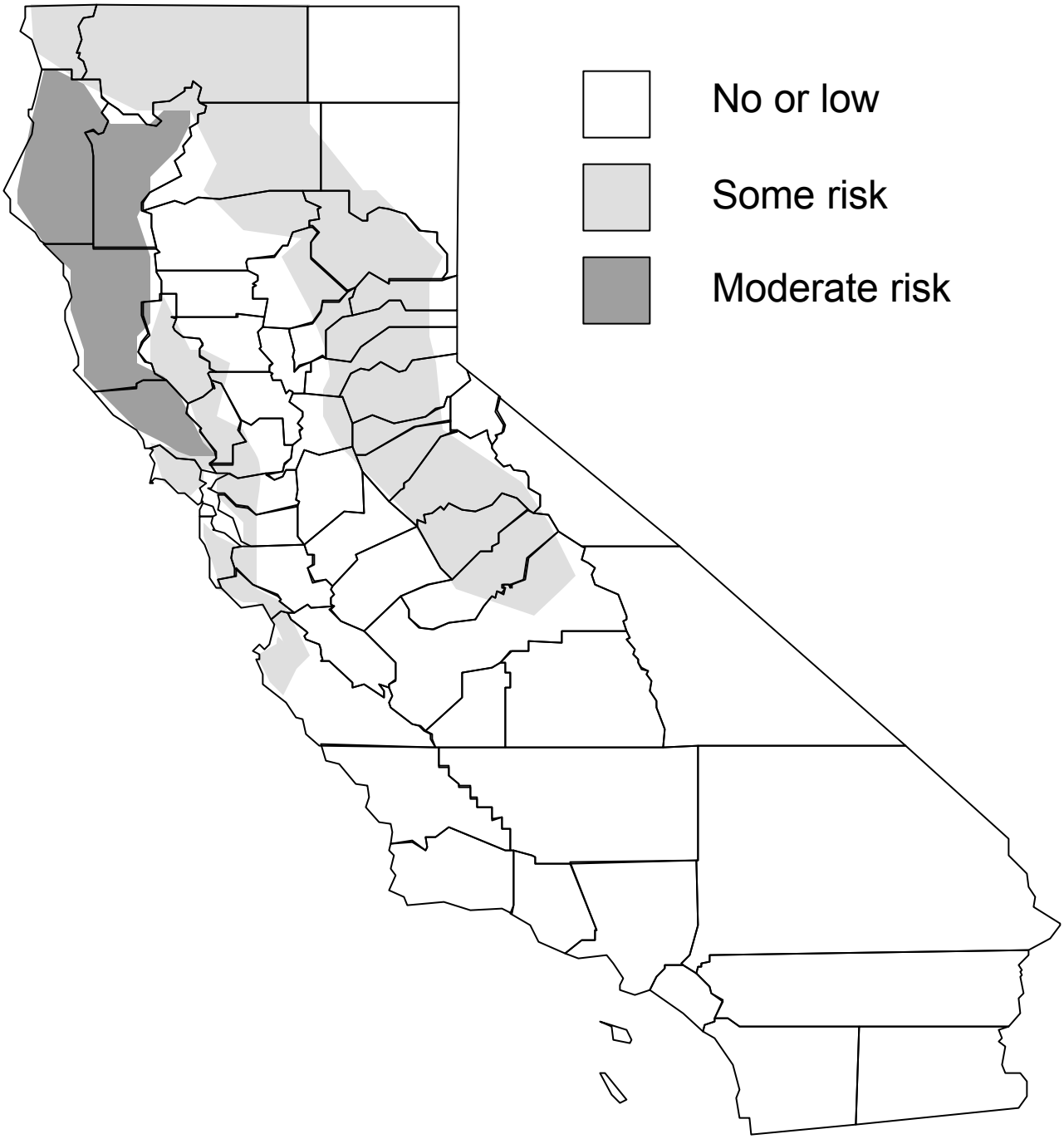
Geographic Area of Risk (see map)

Exposure to Tick Habitat	**Moderate**	**Some**	**Low or None**
Frequent or prolonged	Vaccine *should be* considered	Vaccine *may be* considered	Vaccine *not* recommended
Occurs but is not frequent or prolonged	Vaccine *may be* considered	Vaccine *not* recommended	Vaccine *not* recommended
Minimal or none	Vaccine *not* recommended	Vaccine *not* recommended	Vaccine *not* recommended

Source: California Department of Health Services

Areas of Lyme Disease Risk in California - 1999

(based on reported human cases and Ixodes tick ecology and infection rate)



Source: California Department of Health Services